Citation:

Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, Laranjo N, Leboff MS, Rood JC, de Jonge L, Greenway FL, Loria CM, Obarzanek E, Williamson DA. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med.* 2009; 360 (9): 859-873.

PubMed ID: 19246357

Study Design:

Randomized clinical trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the effects on body weight of energy-reduced diets that differed in their targets for intake of macronutrients, low or high in fat, average or high in protein, or low or high in carbohydrates, following recommendations for cardiovascular health during a period of two years.

Inclusion Criteria:

- *Age:* 30 years to 70 years
- *BMI:* 25 to 40
- 40% men.

Exclusion Criteria:

- Diabetes
- Unstable cardiovascular disease
- Use of medications that affect body weight
- Insufficient motivation assessed by interview or questionnaire.

Description of Study Protocol:

Recruitment

The subjects were recruited through mail where names were identified with the use of lists of registered voters or drivers.

Design

Randomized clinical trial.

- The subjects were randomly assigned to one of four diet groups after eligibility was confirmed
- The nutrient goals of fat, protein and carbohydrates for the four groups were: Low-fat, average-protein; low-fat, high-protein; high-fat, average-protein; high-fat, high-protein
- All diets should include 8% or less of saturated fat, at least 20g dietary fat per day and 150mg of cholesterol per 1,000kcal
- Carbohydrate low glycemic index were recommended for each diet
- Each participant's caloric prescription represented a deficit of 750kcal per day from baseline.
- Similar foods were used for each diet

- Group sessions were held once a week, three of every four weeks during the first six months and two of every four weeks from six months to two years
- Individual sessions were held every eight weeks for the entire two years
- Daily meal plans in two-week blocks were provided
- Participants recorded food and beverage intake in a daily food diary and in a Web-based self-monitoring tool to help them to reach the goals for all macronutrients and energy
- Dietary intake was assessed in a random sample of 50% of the participants by a review of the five-day diet record and by 24-hour recall during a telephone interview on three non-consecutive days
- Questionnaires asking for information on satiety, food craving, eating behavior and satisfaction with diet were applied
- Behavioral counseling and individual sessions were held to promote adherence to the assigned diets
- The goal for physical activity was 90 minutes of moderate exercise per week
- They were monitored by questionnaire and online self-monitoring tool
- Anthropometrics and biochemistry parameters were measured at baseline, six and two years during the intervention.

Blinding Used

Foods were similar for each regimen and staff and investigators who measured outcomes were unaware of the diet assignments for the participants.

Intervention

- *Low-fat, average-protein:* 20% fat, 15% protein, 65% carbohydrate
- *Low-fat, high-protein:* 20% fat, 25% protein, 55% carbohydrate
- *High-fat, average-protein:* 40% fat, 15% protein, 45% carbohydrate
- *High-fat, high-protein:* 40% fat, 25% protein, 35% carbohydrate.

Statistical Analysis

- Data were pooled from the diets from the two factorial comparisons: low-fat vs. high-fat and average-protein vs. high-protein
- Two-sample T-tests at two-sided significance level of 0.05 were used to evaluate independently the effects of protein, fat and carbohydrate levels
- Exploratory post-hoc analyses were performed with threshold amounts of weight loss as outcomes, with Bonferroni's adjustment for multiple comparisons
- Associations between adherence to the fat and protein goals and weight loss were measured using post-hoc analyses
- An intention-to-treat analysis was performed for the long-term weight loss for those participants who withdrew from the study after at least six months of participation
- Risk factors for CVD and diabetes were also performed using an intention-to-treat analysis with zero change from baseline imputed for missing data.

Data Collection Summary:

Timing of Measurements

- Body weight and waist circumference were measured on two days at baseline, six months and two years, and on a single day at 12 and 18 months
- Dietary intake and the questionnaires for eating behavior and satiety were assessed and administered at baseline, six months and two years
- Levels of serum lipids, glucose, insulin, glycated hemoglobin and 24-hour urine samples and measurements of resting metabolic rate were obtained on one day and blood-pressure measurement on two days, at baseline, six months and two years.

Dependent Variables

- Weight (kg)
- BMI
- Waist circumference (cm)
- Blood pressure

- Glucose (mg per dL)
- Insulin (mcg per ml)
- HOMA
- Triglycerides (mg per dL)
- Total cholesterol (mg per dL)
- LDL-cholesterol (mg per dL)
- HDL-cholesterol (mg per dL)
- Urinary nitrogen (g)
- Respiratory quotient.

Independent Variables

- Protein percentage
- Fat percentage
- Carbohydrate percentage
- Total calories.

Control Variables

- Age
- Sex
- Lipid lowering-agents
- Smoking status
- Dietary intake.

Description of Actual Data Sample:

- *Initial N:* 811 (515 females, 296 males)
- *Attrition:* 645 (80%)
- *Age:* Mean age 51
- *Ethnicity:*
    - White, (79%
    - Black, 16%
    - Asian, 1%
    - Hispanic, 4%
    - Other, 1%.

Other Relevant Demographics

- Hypertension was present in 35% of the participants and 28% were using anti-hypertensive drug
- There were 41% smokers and 19% were using some lipid-lowering agents
- Most of the participants (69%) had a high education level (college graduate or beyond)
- The participants were evaluated for the presence of metabolic syndrome
- Serious adverse events were reported by 7% of the participants
- The ratio of microalbuminuria to creatinine was more than 30 in five participants in the average-protein group and in five participants in the average-protein group at six months and in seven participants at two year in the average-protein group.

Anthropometrics

Weight, BMI and waist circumference were similar among the groups. Nevertheless, 73% of the participants were obese with a BMI of 30% or more and 27% overweight with a BMI between 25 to 29.9.

Location

Harvard School of Public Health and Women's Hospital, Boston, Massachusetts and The Pennington Biomedical Research Center of the Louisiana State University System, Baton Rouge, Louisiana.

Summary of Results:

Baseline Characteristics of the Study Participants

Variables	Low-Fat, Average-Protein Group	Low-Fat, High-Protein Group	High-Fat, Average-Protein Group	High-Fat, High-Protein Group	All Participants	Participants who Completed the Study
Weight (kg)	94±16	92±13	92±17	94±16	93±16	93±16
BMI	33±4	33±4	32±4	33±4	33±4	33±4
Waist circumference (cm)	104±13	102±12	103±14	104±13	103±13	104±13
Energy (kcal)	2,015±505	1,862±566	2,012±597	1,979±599	1,966±570	1,978±563
Carbohydrate (%)	44±8	46±8	45±8	44±7	45±8	45±8
Fat (%)	38±6	36±6	37±5	38±6	37±6	37±6
Sat Fat (%)	12±3	12±3	12±3	12±2	12±3	12±3
Protein (%)	18±4	18±4	18±3	18±3	18±3	18±3
Dietary Fiber (g)	18±7	17±7	18±6	17±6	17±7	18±7
Cholesterol (mg)	303±121	278±120	306+135	305±134	298±128	298±128

Weight Loss

- The weight loss after two years was similar in those subjects who consumed a diet with 25% and 15% protein, 3.6kg and 3.0kg, respectively, P=0.22. The same results were observed in those participants whose intake were 40% and 20% fat; 3.3kg in both groups; P=0.94. There was no difference in the weight loss among participants who completed each of these diets. Finally, there was no effect on weight loss of carbohydrate level through the target range of 35% to 65%.
- The change in the waist circumference was not significantly different among the diet groups
- Most of the weight loss (6kg) occurred in the first six months. After 12 months, all groups, on average, slowly regained body weight.
- Among the 80% of participants who completed the trial, the average weight loss was four kg
- At two years, 31% to 37% of the participants had lost at least 5% of their initial body weight, 14% to 15% in each diet group had lost at least 10% of their initial body weight and only 2% to 4% had lost 20kg or more (P>0.2 for the comparisons between diets).

Nutrient Intake According to Diet at Six Months and Two Years

Variables		Energy (kcal)	Carbohydrate (%)	Protein (%)	Fat (%)	Saturated Fat (%)
Low-Fat, Average-Protein Group	*6-month values*	1,636±484	57±11.1	17.6±3.4	26.2±8	7.5±3.2
	Change from baseline	-477	12.8	0.2	-11.8	-4.9
	2-year value	1,531±480	53.2±11	19.6±3.9	26.5±8	8±3.1

	Change from baseline	-554	9.3	2.1	-12.0	-4.3
Low-Fat, High-Protein Group	*6-month values*	1,572±568	53.4±8.5	21.8±3.8	25.9±6.8	7.9±2.7
	Change from baseline	-353	7.4	3.9	-10.1	-3.9
	2-year value	1,560±461	51.3±9.2	20.8±4	28.4±8.1	8.9±3.8
	Change from baseline	-402	6.8	2.5	-8.4	-3.1
High-Fat, Average-Protein Group	*6-month values*	1,607±499	49.1±8.6	18.4±4.5	33.9±6.7	9±2.5
	Change from baseline	-456	5.0	0.5	-3.8	-3.0
	2-year value	1,521±530	48.6±10	19.6±5.2	33.3±8.2	9.8±3.3
	Change from baseline	-434	2.4	2.1	-3.5	-2.1
High-Fat, High-Protein Group	*6-month values*	1,624±484	43±6.7	22.6±4.4	34.3±7.8	9±2.6
	Change from baseline	-385	-0.2	4.3	-3.7	-3.7
	2-year value	1,413±427	42.9±8.3	21.2±5.2	35.1±7	10.5±2.7
	Change from baseline	-389	-0.4	3.4	-3.4	-1.7

PS: P-values are not available on this table in the original article.

Other Findings

- *Risk factors for CDV disease:* At two years, the two low-fat diets and the highest carbohydrate diet decreased LDL-cholesterol, in comparison to the high-fat and lowest-carbohydrates diets; low-fat vs. high-fat, 5% vs. 1%, P=0.001; highest carbohydrate vs. lowest carbohydrate, 6% vs. 1%, P=0.01. The lowest carbohydrate diet increased more the HDL-cholesterol in relation to the highest carbohydrate diet (9% vs. 6%, P=0.02). All diets decreased triglycerides by 12% to 17%. Serum insulin was decreased by 6% to 12% in all diets except the high-carbohydrate diet.
- *Adherence, diet acceptability, satiety and satisfaction:* In the average-protein group there was a larger decrease in urinary nitrogen excretion from baseline, when compared to high-protein group; a difference in the change of 1.6g at six months and 0.8g at two years. In both high- and low-fat groups, the respiratory quotient was 0.84 at baseline and the between-group difference in the change at two years was P=0.002. Diet-satisfaction score was similar at six months and two years among the diets.

- *Attendance and weight change:* Adherence to the goal of protein intake was associated with more weight loss only in the high-protein (24% to 25%) groups and the adherence to the goal for fat intake was associated with more weight loss with the low-fat (25%) groups; P<0.001. Attendance at group sessions was associated with adherence to the fat and protein goals only in these groups.

Author Conclusion:

Reduced-calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize. Such diets can also be tailored to individual patients on the basis of their personal and cultural preferences and may therefore have the best chance for long-term success.

Reviewer Comments:

- *The biggest flaw of this study was the lack of macronutrient dietary intake goals accomplishment. The actual intake of high-protein diet group was only 21% vs. the 25% initially targeted and the low-carbohydrate diet targeted at 35% had an actual intake of 43%.*
- *Only 50% of the participants had the dietary intake assessed which can bring bias to the outcomes*
- *The majority of the population in this study had a higher education degree, were white and were very determined to lose weight. However, authors note that the findings should be directly applicable to both clinicians' recommendations for weight loss in individual patients and the development of population-wide recommendations by public health officials.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	No
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	No
6.6.	Were extra or unplanned treatments described?	No
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	No
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes